

REMARKS

Claims 1, 3-6, 8-15, 20, 24-27, 30 and 31 are pending in the instant application. The Examiner has cited various informalities in claims 1, 8-10, 12, 15, 20 and 31. Claims 4, 5, 27 and 30 stand rejected under 35 USC § 112, second paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 1, 3-6, 8, 9, 11-15, 20, 27 and 30 stand rejected under 35 USC § 112 as being unpatentable over Yu [US 6103492] in view of Buck *et al* ["Photochemically induced dynamic nuclear polarization[...]" Biochemistry 77(9) pp5145-8]. The application has been amended. The claims have been amended. Applicant respectfully submits that none of the amendments introduce new matter in contravention of 35 U.S.C. § 132. Reconsideration is respectfully requested.

Claim Rejections – informalities

The various informalities outlined in respect of claims 1, 8-10, 12, 15, 20 and 31 have been taken into account and the certain suggested amendments have been made.

Applicant respectfully submits that the Examiner's objections to certain terms, namely 'hyperpolarising', 'hyperpolarisation', 'analysing', 'analysed', 'hybridisation', 'polarisation', etc., are improper as each of these terms is well understood in the English language and as used in the instant application. As support, Applicant submits photocopied pages 41 and 900 of Merrian-Webster's Collegiate Dictionary, Tenth Edition, for definitions of the words 'analyse' and 'polarize' showing that each are simply British variants of 'analyze' and 'polarize'. Additionally, Applicant directs the Examiner's attention to United States Patent Nos. 7,186,550 and 7,107,169 as merely two examples of the word 'hybridisation' being used in the very first issued claim. Applicant notes that many more patents have issued using these very same terms in their claims, indicating their acceptability.

In view of the amendments and remarks hereinabove, it is respectfully submitted that each of the noted objections have either been obviated by amendment or traversed as being improper. Reconsideration and withdrawal of the objections is respectfully requested.

Claim Rejections – 35 USC § 112

Claims 4, 5, 27 and 30 are rejected under 35 USC § 112, second paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 4 and 5 have been amended such that the term “artificially high concentration” has been replaced with the term “artificially-enriched abundance”. The replacement term finds basis in the application as filed on page 3 lines 25-28 as well as on page 6 lines 15-32. Applicant submits that the teaching of the specification provides ample guidance to the skilled person as to what the term “artificially-enriched abundance” means.

Claim 27 has been amended such that the wording reflects that in the specification as filed on page 17 lines 30-32. Applicant submits that “no well, surface or container” does not require antecedent basis as re-worded and also that the phrase now clearly applies only to the aerosol.

Claim 30 in its present form is not regarded by Applicant as being indefinite for the reasons outlined by the Examiner. Applicant respectfully submits that the Examiner’s argumentation is flawed in that claim 30 does not encompass both a broad range and a narrow range. Claim 30 definitively encompasses one preferred value from the range set out in claim 5, i.e. “one specific position” as a preferred value from “up to 10 defined positions”. It is Applicants belief that the limitation of claim 30 is thus abundantly clear to one of ordinary skill in the art.

In view of the amendments and remarks hereinabove, Applicant respectfully submits that each rejection under 35 USC § 112, second paragraph has been traversed. Reconsideration and withdrawal of the rejections are respectfully requested.

Claim Rejections – 35 USC § 103

Claims 1, 3-6, 8, 9, 11-15, 20, 27 and 30 are rejected under 35 USC § 112 as being unpatentable over Yu [US 6103492] in view of Buck *et al* [“Photochemically induced dynamic nuclear polarization[...]” Biochemistry 77(9) pp5145-8]. The rejection is respectfully traversed.

As stated by the Examiner, neither Yu nor Buck teach that the degree of hyperpolarisation of the NMR active nucleus is in excess of 0.1%. However, the Examiner contends that to get from the combined teachings of Yu and Buck to the subject matter of claim 1, the skilled person would only need to use routine skill in the art. In response to Applicant’s previous arguments filed September 18 2006, the Examiner is not persuaded that claim 1 is inventive over the teachings of the prior art. The Examiner contends that the assay performed by Buck is only an example of a hyperpolarisation assay rather than being a limitation on the technique disclosed by Buck. The Examiner further contends that there is no showing by the Applicant that the hyperpolarisation technique is any different from that disclosed by Buck.

Applicant respectfully contends this assertion. The method of Buck is photochemically-induced dynamic nuclear polarization [CIDNP] in which the NMR signal intensity is enhanced by contact of a sample with a photoexcited dye. As presented in Applicant’s response dated September 18 2006, the level of polarization achievable with this method is in the order of 0.6% above equilibrium. Furthermore, for the assay of Buck, this method of enhancing polarization is particularly suitable as it specifically enhances the NMR signal intensities of the aromatic amino acids that the assay of Buck wishes to analyze [see page 5145 column 2 second paragraph of Buck]. In the present invention, hyperpolarisation may be carried out using a variety of techniques, such as polarisation transfer from a noble gas, “brute force”, DNP and the para-hydrogen method. As outlined in detail on page 1 line 31 to page 2 line 29, all of these methods are qualitatively different from CIDNP in that they do not involve contact of the sample with a photoexcited dye. These hyperpolarisation methods are all capable of achieving polarisation levels of at least 0.1% above equilibrium.

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Amdt. Dated April 3, 2007
Reply to Office action of October 4, 2006

Applicant therefore respectfully contends that the polarisation technique presented by Buck is different to those presented in the present invention. In addition, given that the polarisation technique of Buck is particularly suited to the assay described therein, the skilled person would not be motivated to use a different polarisation method. For these reasons, Applicant respectfully submits that claim 1 of the present invention is patentably distinct over Yu in view of Buck and respectfully requests that the rejection should be withdrawn.

All the arguments presented by the examiner in rejection of claims 3-6, 8, 9, 11-15, 20, 27 and 30 are based on the premise that claim 1 is unpatentable over Yu in view of Buck. Applicant respectfully submits that as claim 1 is patentable over Yu in view of Buck for the reasons presented above, each of claims 3-6, 8, 9, 11-15, 20, 27 and 30 are also patentable over the cited prior art. Reconsideration and withdrawal of these rejections are respectfully requested.

In view of the amendments and remarks hereinabove, Applicant respectfully submits that the instant application, including claims 1, 3-6, 8, 9, 11-15, 20, 27, and 30, is allowable over the prior art. Favorable action thereon is respectfully requested.

Any questions with respect to the foregoing may be directed to Applicant's undersigned counsel at the telephone number below.

Respectfully submitted,

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UPDATED ANNUALLY

**Merriam-
Webster's
Collegiate
Dictionary**

TENTH EDITION

- Clear and precise
- Best guidance on word choice
- Most definitions—over 215,000

water) reclaimed from a body of water (as the sea)

various minor offenses (as breach of the peace) and the power

campaigns of candidates likely to advance the group's interests

one of the four basal ganglia in each of the limbic system and consists of an latter in the anterior extremity of the *gdaloid nucleus*
ila (1651): a white crystalline cyanound esp. in the seeds of the apricot.

mygdalocides, fr. *amygdalē* (1836) 1 g to, or affecting an amygdala
dy adj (1813): of, being, or contain- k that are filled with deposits of differ- calcite) — *amyg-da-lold* \ə-ˈmīg-də-

3-y] (1850): a univalent hydrocarbon various isomeric forms and is derived

, *amylum*, fr. Gk *amylon*, fr. neut. of *a-* + *mylē* mill — more at MEAL]

ANA OIL
 eight isomeric alcohols C₈H₁₈O used sters; also: a commercially produced p. as a solvent
 893): any of a group of enzymes (as lyolysis of starch and glycogen or their
 ale yellow pungent flammable liquid myl alcohol and nitrous acid — com-

axy translucent substance consisting of ysaccharides that is deposited in some abnormal conditions (as Alzheimer's

\ n [NL] (ca. 1900): a disorder char- yoid in bodily organs and tissues
 idj [NL] *amylolysis*, fr. *amyl-* + *-lysis* apable of the enzymatic splitting of zymes) (~ activity)
 \ n (1905): a component of starch and branched structure and does not

\ n (1886): a colorless plastid that

[*amyl-* + *-psin* (as in *trypsin*)] (ca. atic juice
 877): a component of starch charac- ucose units
 [NL] (ca. 1919): deficiency of mus-

is \a-mi-a-ˈtrō-fik-, -ˈtrā- \ n [a- + are progressive degenerative fatal dis- u, beginning in middle age, and char- preading muscular weakness — called

— used for amobarbital
 ME, fr. OE *an* one — more at ONE]

usage see *AN*
 : AND 2 \an\ archaic: IF

n & -ian fr. ME *-an*, -ian, fr. OF & L. nus, fr. -anus, adj. suffix: -ean fr. such an] 1: one that is of or relating to skilled in or specializing in (phoneti-

1: of or belonging to (American): resembling (Mozartean)
 : of -ene, -ine & -one] 1: unsaturated hydride of a carbohydrate (dextran) Gk. at the rate of, lit., up] (14c): of prescriptions

nas [ˈana] (ca. 1751) 1: a collection rson 2: a collection of anecdotes or erson or a place
 back, again, fr. *ana* up — more at OK] : back: backward (anotropic)
 L, neut. pl. of -anus -an & -ianus -ian] esp. anecdotal or bibliographical con-

\ n [NL] *anabaptism*, fr. LGk *ana-* baptize, fr. Gk *ana-* again + *p-* a: the doctrine or practices of the t movement 2: the baptism of one

): a Protestant sectarian of a radical tury and advocating the baptism and lievers only, nonresistance, and the *Anabaptist* adj
a-ses \sēz\ [Gk. inland march, fr. *ana-* + *bainein* to go — more at *ADVANCE*; esp.: a mix- of Greek mercenaries in Asia Minor nophon]: a difficult and danger-

Gk *anabatos*, verbal of *anabainein* (an ~ wind)
 of a group of usu. synthetic hormone- olism and are sometimes abused to pparately the size of their muscles
 [SV *ana-* + *metabolism*] (1860): its- concerned esp. with macromolecu- — *an-a-bol-ic* \a-na-ˈbō-lik\ adj
 \ n [prob. fr. MGk *anachronismos*, t- onism, fr. LGk *anachronizein* to be

late, fr. Gk *ana-* + *chronos* time] (ca. 1646) 1: an error in chronol- ogy; esp.: a chronological misplacing of persons, events, objects, or customs in regard to each other 2: a person or a thing that is chrono- logically out of place; esp.: one from a former age that is incongruous in the present — *anach-ro-nis-tic* \a-na-kra-ˈnis-tik\ also *ana-chron- ic* \a-na-ˈkrā-nik\ adj — *anach-ro-nis-ti-cal-ly* \a-na-kra-ˈnis-ti- k(ə)-lē\ adv — *anach-ro-nous* \a-ˈna-kra-nəs\ adj — *anach-ro-nous- ly* adv

an-a-clit-ic \a-na-ˈkli-tik\ adj [Gk *anaklitos*, verbal of *anaklinein* to lean upon, fr. *ana-* + *klinein* to lean — more at LEAN] (1922): of, relating to, or characterized by the direction of love toward an object (as the mother) that satisfies nonsexual needs (as hunger)

an-a-co-lu-thon \a-na-kə-ˈlū-thən\ n, pl -thas also -thons [L.L. fr. LGk *anakolouthon* inconsistency in logic, fr. Gk, neut. of *anako- louthos* inconsistent, fr. *an-* + *akolouthos* following, fr. *ha-*, *a-* together + *keleuthos* path] (ca. 1706): syntactical inconsistency or incoherence within a sentence; esp.: a shift in an unfinished sentence from one syn- tactic construction to another (as in "you really ought—well, do it your own way") — *an-a-co-lu-thic* \-thik\ adj — *an-a-co-lu-thi-cal- ly* \-thik(ə)-lē\ adv

an-a-con-da \a-na-ˈkän-də\ n [prob. modif. of *anahalese henakandayā*, a slender green snake] (1768): a large semiaquatic constricting snake (*Unectes murinus*) of the boa family of tropical A. America that may reach a length of 30 feet (9.1 meters); broadly: any of the large constrict- ing snakes

an-a-re-on-tic \a-na-kre-ˈän-tik\ n (1656): a poem in the manner of Anacreon; esp.: a drink- ing song or light lyric

Anacreontic adj [L *anacreonticus*, fr. *Anacreont-*, *Anacreon* Anacreon, fr. Gk *Anakreont-*, *Anakreon*] (1611) 1: of, relating to, or resembling the poetry of Anacreon 2: convivial or amatory in tone or theme

an-a-cru-sis \a-na-ˈkrū-səs\ n, pl -cru-ses \-sēz\ [L, fr. Gk *anakrousis* beginning of a song, fr. *anakrouein* to begin a song, fr. *ana-* + *krouein* to strike, beat; akin to Lith *krausyti* to strike] (1830) 1: one or more syllables at the beginning of a line of poetry that are regarded as preliminary to and not a part of the metrical pattern 2: UPBEAT, specif.: one or more notes or tones preceding the first downbeat of a musical phrase

an-a-dama bread \a-na-ˈda-mə\ n [origin unknown] (1954): a leav- ed bread made with flour, cornmeal, and molasses

an-a-dem \a-na-dem\ n [L *anadema*, fr. Gk *anadēma*, fr. *anadein* to weathe, fr. *ana-* + *dein* to bind — more at DIADEM] (1604) archaic: a wreath for the head: GARLAND

an-a-diplo-sis \a-na-ˈdī-plō-sis, -a-na-(dī)-plō-sis\ n, pl -plo-ses \-sēz\ [L, fr. Gk *anadiplosis*, lit., repetition, fr. *anadiploin* to double, fr. *ana-* + *diploin* to double — more at DIPLOMA] (ca. 1550): repetition of a word or phrase, the last word in one phrase or clause at the begin- ning of the next (as in "rely on his honor—honor such as his?")

an-a-ro-mous \a-na-ˈdra-məs\ adj [Gk *anadromos* running upward, fr. *anadromēin* to run upward, fr. *ana-* + *dramein* to run — more at *ANADROMY*] (ca. 1753): ascending rivers from the sea for breeding (as salmon) — compare CATADROMOUS

an-a-emia, *an-aemic* chiefly Brit var of ANEMIA, ANEMIC

an-a-robe \a-na-rōb; (Jan-ˈa-ˈrōb, -ˈe-ˈrōb\ n [ISV] (1884): an anabolic organism

an-a-ro-bic \a-na-ˈrō-bik; Jan-ˈa-(ə)-, -ˈe-(ə)-\ adj (ca. 1881) 1 a : requiring active, occurring, or existing in the absence of free oxygen (as fermentation) b : of, relating to, or being activity in which the body uses an oxygen debt (~ exercise) 2: relating to or induced by anaerobes — *an-aer-o-bi-cal-ly* \-bi-k(ə)-lē\ adv

an-a-ro-bi-o-sis \a-na-ˈrō-(bī)-ō-sis, -bē-, -ˈe-(ə)-\ n, pl -o-ses \-sēz\ [NL] (ca. 1889): life in the absence of air or free oxygen

an-a-es-the-sia, *an-aes-the-tic* chiefly Brit var of ANESTHESIA, ANES-

an-a-es-the-sis \a-na-ˈje-ne-səs\ n [NL] (1889): evolutionary change involving a single lineage in which one taxon replaces another without branching — compare CLADOGENESIS

an-a-glyph \a-na-ˈglif\ n [LL *anaglyphus* embossed, fr. Gk *anaglyphos*, *anaglyphein* to emboss, fr. *ana-* + *glyphein* to carve — more at *GLYPH*] (1651) 1: a sculptured, chased, or embossed ornament used in low relief 2: a stereoscopic motion or still picture in which each component of a composite image usu. red in color is superimposed on the left component in a contrasting color to produce a three-dimensional effect when viewed through correspondingly colored fil- ter in the form of spectacles — *an-a-glyph-ic* \a-na-ˈgli-fik\ adj

an-a-gnō-ris-is \a-na-ˈgnō-ris-səs\ n, pl -ri-ses \-sēz\ [Gk *anagnōris-*, *anagnōrissein* to recognize, fr. *ana-* + *gnōrissein* to make known; akin to *anagnōris* well-known, *gignōrissein* to come to know — more at *AGNATE*] (1800): the point in the plot esp. of a tragedy at which the protagonist recognizes his or her or some other character's true iden- tity — more at *ANAGNORISIS*

an-a-go-gy \a-na-ˈgō-jē\ n, pl -gies or -gies [LL *anagoge*, fr. Gk. reference, fr. *anagein* to refer, fr. *ana-* + *gōgē* to lead — more at AGENT] (15c): interpretation of a word, pas- sage, text (as of Scripture or poetry) that finds beyond the literal, moral, and moral senses a fourth and ultimate spiritual or mystical meaning — *an-a-go-gic* \a-na-ˈgō-jik\ or *an-a-go-gi-cal* \-ji-kəl\ adj — *an-a-go-gi-cal-ly* \-ji-k(ə)-lē\ adv

an-a-gram \a-na-ˈgram\ n [prob. fr. MF *anagramme*, fr. NL *anagram-*, *anagramma*, modif. of Gk *anagrammatismos*, fr. *anagram-* + *matismos* to transpose letters, fr. *ana-* + *grammat-*, *gramma* letter — more at GRAM] (1589) 1: a word or phrase made by transposing the letters of another word or phrase 2 pl but sing in constr.: a game in which words are formed by rearranging the letters of other words or by transposing letters taken (as from a stock of cards or blocks) at random

an-a-gram-matic \a-na-ˈgra-ˈma-tik\ also *an-a-gram-mat-i-cal* \-ti-k(ə)-lē\ adj

an-a-gram-mat-i-cal-ly \-ti-k(ə)-lē\ adv



anaconda

anagram vt -grammed; -gram-ming (1630) 1: ANAGRAMMATIZE 2 : to rearrange (the letters of a text) in order to discover a hidden mes- sage

an-a-gram-ma-tize \a-na-ˈgra-mə-ˈtiz\ vt -tized; -tiz-ing (1588): to transpose (as letters in a word) so as to form an anagram — *an-a-gram-ma-ti-za-tion* \-gra-mə-tə-ˈzā-shən\ n

anal \ˈa-nəl\ adj (1769) 1: of, relating to, or situated near the anus (~ fin) 2 a: of, relating to, characterized by, or being the stage of psy- chosexual development in psychoanalytic theory during which the child is concerned esp. with its feces b: of, relating to, characterized by, or being personality traits (as parsimony, meticulousness, and ill humor) considered typical of fixation at the anal stage of development (~ disposition) (~ neatness) — *anal-ly* \-nəl-ē\ adv

anal-cime \ˈa-nəl-sēm\ n [F, fr. Gk *anakimos* weak, fr. *an-* + *alkimos* strong, fr. *alkē* strength] (1803): a white or slightly colored mineral that consists of hydrated silicate of sodium and aluminum and occurs in various igneous rocks in massive form or in crystals

anal-cite \ˈa-nəl-sī\ n (1868): ANALCIME

an-a-lects \a-nəl-ˈek(t)s\ also *an-a-lect-ta* \a-nəl-ˈek-tə\ n pl [NL *ana-* lecta, fr. Gk *analekta*, neut. pl. of *analektos*, verbal of *analegein* to collect, fr. *ana-* + *legein* to gather — more at LEGEND] (1652): selected miscellaneous written passages

an-a-lem-ma \a-na-ˈle-mə\ n [L, sundial on a pedestal, fr. Gk *analemma*, lofty structure, sundial, fr. *analembainein* to take up, re- store, fr. *ana-* + *lambainein* to take — more at LATCH] (1832): a plot or graph of the position of the sun in the sky at a certain time of day (as noon) at one locale measured at regular intervals throughout the year that has the shape of a figure 8; also: a scale (as on a globe or sundial) based on such a plot that shows the sun's position for each day of the year or that allows local mean time to be determined — *an-a-lem-mat- ic* \a-na-ˈle-ˈma-tik, -lə\ adj

an-a-lep-tic \a-na-ˈlep-tik\ n [Gk *analeptikos*, fr. *analembainein*] (1671): a drug that stimulates the central nervous system — *analeptic* adj

an-al-ge-sia \a-nəl-ˈjē-zh(ē)-, -zē-ə\ n [NL, fr. Gk *analgesia*, fr. *an-* + *algēsis* sense of pain, fr. *algēin* to suffer pain, fr. *algos* pain] (ca. 1706): insensibility to pain without loss of consciousness — *an-al-ge-sic* \-jē-zik, -sik\ adj or n — *an-al-ge-si-ty* \-jē-tik\ adj or n

anal-i-ty \a-na-ˈla-tē\ n, pl -ties (1939): the psychological state or quality of being anal

an-a-log \a-nəl-ˈŏg, -äg\ adj (1948) 1: of, relating to, or being an analogue 2 a: of, relating to, or being a mechanism in which data is represented by continuously variable physical quantities b: of or relating to an analog computer c: being a timepiece having hour and minute hands

analog computer n (1948): a computer that operates with numbers represented by directly measurable quantities (as voltages or rotations) — compare DIGITAL COMPUTER, HYBRID COMPUTER

an-a-log-i-cal \a-nəl-ˈŏ-jī-kəl\ also *an-a-log-ic* \-jī-k\ adj (1609) 1 : of, relating to, or based on analogy 2: expressing or implying analogy — *an-a-log-i-cal-ly* \-jī-k(ə)-lē\ adv

an-a-log-ist \a-na-ˈlŏ-jist\ n (ca. 1828): one who searches for or reasons from analogies

an-a-log-ize \-jīz\ vb -gized; -giz-ing w (1655): to use or exhibit analogy ~ vt: to compare by analogy

an-a-log-ous \a-na-ˈlŏ-gəs\ adj [L *analogus*, fr. Gk *analogos*, lit., proportionate, fr. *ana-* + *logos* reason, ratio, fr. *legein* to gather, speak — more at LEGEND] (1646) 1: showing an analogy or a likeness that permits one to draw an analogy 2: being or related to as an analogue SYN see SIMILAR — *an-a-log-ous-ly* adv — *an-a-log-ous-ness* n

an-a-logue or *an-a-log* \a-nəl-ˈŏg, -äg\ n [F *analogue*, fr. *analogue* analogous, fr. Gk *analogos*] (1826) 1: something that is analogous or similar to something else 2: an organ similar in function to an organ of another animal or plant but different in structure and origin 3 *usu* *analog*: a chemical compound that is structurally similar to another but differs slightly in composition (as in the replacement of one atom by an atom of a different element or in the presence of a particular functional group) 4: a food product made by combining a less expen- sive food (as soybeans or whitefish) with additives to give the appear- ance and taste of a more expensive food (as beef or crab)

an-a-logue chiefly Brit var of ANALOG

an-a-lo-gy \a-na-ˈlŏ-jē\ n, pl -gies (15c) 1: inference that if two or more things agree with one another in some respects they will prob- ably agree in others 2 a: resemblance in some particulars between things otherwise unlike b: comparison based on such resem- blance 3: correspondence between the members of pairs or sets of linguistic forms that serves as a basis for the creation of another form 4: correspondence in function between anatomical parts of different structure and origin — compare HOMOLOGUE SYN see LIKENESS

an-al-pha-bet \ˌan-ˈal-fə-ˈbet, -bət\ n [Gk *analphabētos* not knowing the alphabet, fr. *an-* + *alphabētos* alphabet] (ca. 1889): one who cannot read: ILLITERATE — *an-al-pha-bet-ic* \ˌan-ˈal-fə-ˈbet-ik\ adj or n

an-al-pha-bet-ism \ˌan-ˈal-fə-ˈbi-tiz-əm\ n

an-a-ly-sand \a-na-ˈlŏ-sənd\ n [*analyse* + *-and* (as in *multiplicand*)] (1917): one who is undergoing psychoanalysis

an-a-lyse chiefly Brit var of ANALYZE

an-a-ly-sis \a-na-ˈlŏ-səs\ n, pl -yses \-sēz\ [NL, fr. Gk, fr. *analysein* to break up, fr. *ana-* + *lyein* to loosen — more at LOSE] (1581) 1: separa- tion of a whole into its component parts 2 a: the identification or separation of ingredients of a substance b: a statement of the constitu- ents of a mixture 3 a: proof of a mathematical proposition by assuming the result and deducing a valid statement by a series of re- versible steps b (1): a branch of mathematics concerned mainly with functions and limits (2): CALCULUS 1b 4 a: an examination of a complex, its elements, and their relations b: a statement of such an analysis 5 a: a method in philosophy of resolving complex expres- sions into simpler or more basic ones b: clarification of an expression by an elucidation of its use in discourse 6: the use of function words

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an-a-ly-sis chiefly Brit var of ANALYZE



US007107169B2

(12) **United States Patent**
Vary

(10) **Patent No.:** **US 7,107,169 B2**
(45) **Date of Patent:** **Sep. 12, 2006**

(54) **DEVICE FOR ESTIMATING THE MASS FLOW OF FUEL**

(75) Inventor: **Florian Vary**, Melun (FR)

(73) Assignee: **Snecma Moteurs**, Paris (FR)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 133 days.

(21) Appl. No.: **10/911,521**

(22) Filed: **Aug. 5, 2004**

(65) **Prior Publication Data**

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(30) **Foreign Application Priority Data**

Aug. 22, 2003 (FR) 03 10106

(51) **Int. Cl.**

G01F 1/12 (2006.01)

G01F 1/50 (2006.01)

(52) **U.S. Cl.** **702/100**; 702/45; 73/1.16;
73/1.34; 700/282

(58) **Field of Classification Search** 702/98,
702/100, 13, 8; 73/1.16, 1.19, 1.21, 1.23,
73/1.34, 1.35, 1.57, 1.59, 861, 861.01, 861.42;
700/282-285

See application file for complete search history.

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(74) *Attorney, Agent, or Firm*—Oblon, Spivak, McClelland, Maier & Neustadt, P.C.

(57) **ABSTRACT**

The invention relates to a device for determining a measurement of mass flow of fluid for a combustion chamber comprising a fluid metering device and a means of measuring the position of the metering device being measured. This device comprises:

a mass flow meter,

a hybridisation device for determining an actual mass flow of fluid comprising:

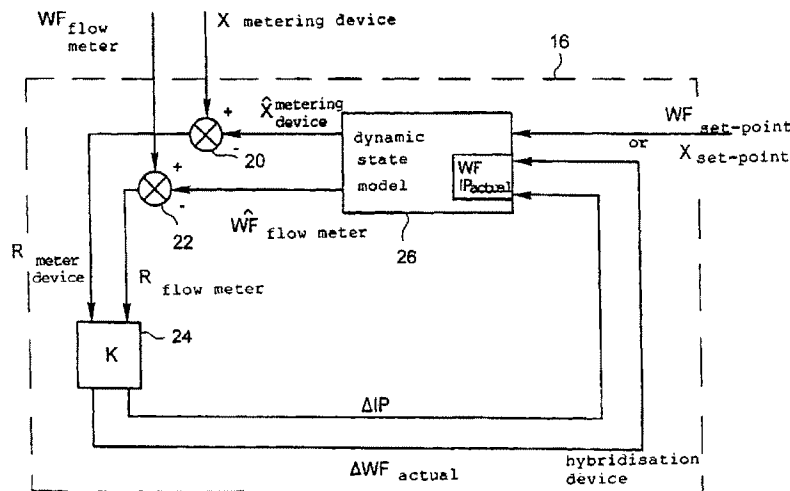
a first input comprising a set-point value (WF set-point, Xset-point),

a prediction unit (26) capable of determining, from the first input and variables of state comprising the actual mass flow (WF actual) and parametric unknowns (IP), estimated values (\hat{WF} flow meter, \hat{X} metering device), a second input comprising the measured position of the metering device (X metering device) and the measured mass flow of fluid (WF flow meter),

a calculator of residues (30, 22, 20) for determining a first residue (R metering device) between the measured position of the metering device and the estimated position of the metering device and a second residue (R flow meter) between the measured mass flow of fluid and the estimated mass flow of fluid,

a correction unit (24) for determining, from the first and second residues corrections capable of being applied to variables of state (WF actual, IP).

18 Claims, 4 Drawing Sheets



-continued

$$A8- Z = \left[\frac{WF_{actual}}{IP} \right]$$

$$A9- Y = \left[\frac{\dot{W}F_{flow_meter}}{\dot{X}_{metering_device}} \right]$$

$$A10- U = [WF \text{ set-point or } X \text{ set-point}]$$

$$A11- Z_{n+1} = F \cdot Z_n + U_n$$

$$Y_{n+1} = H \cdot Z_n$$

A12 NOTATIONS

Xconsigne: metering device position sought

WFconsigne: mass fuel flow sought

WFreeel: mass flow actually delivered by the metering system

WFdebitmetre mass flow measured by the flow meter

^WFdebitmetre estimated mass flow

ΔWFreeel correction of actual mass flow

Xdoseur measured position of the metering device slide valve

^Xdoseur estimated position of the metering device slide valve

Rdebitmetre residue of mass flow

Rdoseur residue of the position of the metering device slide valve

IP vector of parametric unknowns

ΔIP correction vector of vector of parametric unknowns

K correction gain matrix

z vector of state of filter

Y vector of estimated outputs

U vector of set-point inputs

H output matrix

F state matrix

Q matrix of covariance of the state interference

v state interference

R matrix of covariance of measurement interference

w measurement interference

What is claimed is:

1. A device for determining a measurement of mass fluid flow for a combustion chamber comprising a fluid metering device and a means of measuring the position of metering device known as the measured position, said device comprising:

a mass flow meter for measuring a mass flow of fluid known as the measured flow,

a hybridisation device suitable for determining an actual mass flow of fluid comprising:

a first input comprising a set-point value (WFset-point) of the mass flow sought or a set-point value (Xset-point) of the position of the metering device sought, a prediction unit capable of determining, from the first input and variables of state comprising the actual mass flow (WFactual) and parametric unknowns (IP), estimated values comprising the estimated position of the metering device (^Xmetering device) and the estimated mass flow (AWF flow meter),

a second input comprising the measured position of the metering device (Xmetering device) and the measured fluid mass flow (WFflow meter),

a calculator of residues capable of determining a first residue (Rmetering device) between the measured position of the metering device and the estimated

position of the metering device and a second residue (Rflow meter) between the measured fluid mass flow and the estimated fluid mass flow,

a correction unit capable of determining from the first and second residues corrections capable of being applied by the prediction unit to the variables of state (Wfactual, IP).

2. A device according to claim 1, wherein the prediction unit comprises a dynamic model at the state linking the first input to the variables of state and estimated values.

3. A device according to claim 1, wherein the correction unit comprises a correction gain matrix whose coefficients are fixed.

4. A device according to claim 1, wherein the correction unit comprises a correction gain matrix whose coefficients are variable.

5. A device according to claim 1, wherein the correction unit comprises a correction gain matrix whose coefficients are variable and the coefficients are determined by a mathematical law dependent on the mass flow of fluid or on the position of the metering device.

6. A device according to claim 1, wherein the correction unit comprises a correction gain matrix whose coefficients are variable and the correction gain matrix is a gain matrix of the Kalman filter (K), determined dynamically.

7. A device according to claim 1, wherein the correction unit comprises a correction gain matrix whose coefficients are variable the correction gain matrix is a gain matrix of the Kalman filter (K), determined dynamically by the use of matrices relating to the interference, submitted to continuous adaptation of their coefficients.

8. A device according to claim 1, wherein the first input further comprises a measured value of the temperature of the fluid (Tfuel).

9. A device according to claim 1, wherein the second input comprises a measured value of a pressure differential through the fluid metering device (^δPmeasurement), the estimated values comprise an estimated value of this pressure differential (^δPmeasurement), the residue calculator is capable of determining a third residue (RδP), between the measured value and the estimated value of the pressure differential, and the correction unit is capable of determining, from the first, second and third residues, corrections suitable for application by the prediction unit to the variables of state.

10. A process of determining a measurement of mass flow of a fluid for a combustion chamber, said process comprising the steps of:

a- entering a set-point value (WFset-point) of the mass flow sought or a set-point value (X set-point) of the position of the metering device sought, and variables of state comprising the actual mass flow (WF actual) and parametric unknowns (IP),

b- determining from step a- estimated values comprising the estimated position of the fluid metering device (^X metering device) and the estimated mass flow (^WF-flow meter),

c- measuring the mass flow of fluid (WFflow meter) from a mass flow meter and the position of the fluid metering device (Xflow meter),

d- calculating a first residue (Rmetering device) between the measured position of the metering device and the estimated position of the metering device and a second residue (Rflow meter) between the measured mass flow of fluid and the estimated mass flow of fluid,



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(12) **United States Patent**
Choo et al.

(10) **Patent No.:** **US 7,186,550 B2**

(45) **Date of Patent:** ***Mar. 6, 2007**

(54) **NUCLEIC ACID MOLECULE**

(75) Inventors: **Kong-Hong Andy Choo**, Doncaster East (AU); **Desiree Du Sart**, Doncaster (AU); **Michael Robert Cancilla**, Maribyrnong (AU)

(73) Assignee: **Murdoch Childrens Research Institute**, Parkville (AU)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 296 days.

This patent is subject to a terminal disclaimer.

(21) Appl. No.: **09/728,552**

(22) Filed: **Dec. 2, 2000**

(65) **Prior Publication Data**

US 2003/0096398 A1 May 22, 2003

Related U.S. Application Data

(63) Continuation of application No. 09/078,294, filed on May 13, 1998, now Pat. No. 6,265,211.

(30) **Foreign Application Priority Data**

May 13, 1997 (AU) PO6784
Aug. 26, 1997 (AU) PO8791

(51) **Int. Cl.**

C12N 15/63 (2006.01)

C07H 21/04 (2006.01)

(52) **U.S. Cl.** **435/320.1; 536/23.1**

(58) **Field of Classification Search** **435/320.1; 536/23.1, 24.1; 514/44**

See application file for complete search history.

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Primary Examiner—Celine Qian

(74) *Attorney, Agent, or Firm*—Scully, Scott, Murphy & Presser, P.C.

(57) **ABSTRACT**

The present invention is directed generally to an isolated nucleic acid molecule encompassing a neocentromere or a functional derivative thereof or a latent, synthetic or hybrid form thereof and its use inter alia in developing a range of eukaryotic artificial chromosomes including mammalian (e.g. human) and non-mammalian an artificial chromosomes. Such artificial chromosomes are useful in a range of genetic therapies.

20 Claims, 223 Drawing Sheets

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| | |
|--|-----|
| taaaaaagtt gacgtgtata atccatgtaa aaaagttggc agaagagaca aactggtaaa | 300 |
| gcagccggttc ttcatatttc atttcattca acaagcatta ttaacagcct agcaagaaca | 360 |
| cagtatccag gaaaaatcaa agattatcaa gtcctatgtc tataatcaag caatttataa | 420 |
| actagcagaa gaacaagaca gatgaataag aacttgggta tatttaaatg ctaagaagtt | 480 |
| caattcaaat aaatgtcc | 498 |

The invention claimed is:

1. An isolated nucleic acid molecule comprising a neocentromere, wherein said neocentromere comprises a region of an eukaryotic chromosome and does not have any detectable alpha satellite DNA as determined by fluorescent in situ hybridisation (FISH), wherein said nucleic acid molecule comprises SEQ ID NO: 3, and wherein said nucleic acid molecule, when introduced into a cell, is capable of replicating, acting as an extra-chromosomal element and segregating with cell division.
2. The isolated nucleic acid molecule according to claim 1 wherein the eukaryotic chromosome is a mammalian chromosome.
3. The isolated nucleic acid molecule according to claim 2 wherein the chromosome is a human chromosome.
4. The isolated nucleic acid molecule according to claim 2 wherein the nucleic acid molecule binds to centromeric binding proteins (CENP)-A and -C or antibodies thereto.
5. The isolated nucleic acid molecule according to claim 3 wherein the chromosome is human chromosome 10.
6. The isolated nucleic acid molecule according to claim 5 wherein said neocentromere comprises a region mapping between q24 and q26 on said human chromosome 10.
7. The isolated nucleic acid molecule according to claim 3 wherein said human chromosome is a mardel (10) chromosome.
8. The isolated nucleic acid molecule of claim 1 wherein said nucleic acid molecule is in linear form and co-introduced into a cell together with a telomeric sequence.
9. The isolated nucleic acid molecule according to claim 8 wherein the eukaryotic chromosome is a mammalian chromosome.
10. The isolated nucleic acid molecule according to claim 9 wherein said nucleic acid molecule binds to CENP-A and CENP-C antibodies.
11. The isolated nucleic acid molecule according to claim 9 wherein the mammalian chromosome is human chromosome 10.
12. The isolated nucleic acid molecule according to claim 11 wherein the neocentromere comprises a region mapping between q24 and q26 on said human chromosome 10.
13. The isolated nucleic acid molecule according to claim 8 wherein said chromosome is a human mardel (10) chromosome.
14. A genetic construct comprising an origin of replication for a eukaryotic cell and the nucleic acid molecule of claim 1, operably linked to telomeric nucleotide sequences functional in the cell in which the genetic construct is to replicate and wherein said genetic constructs when introduced into a cell, is a replicating, extra-chromosomal element which segregates with cell division.
15. The genetic construct according to claim 14 wherein the eukaryotic chromosome is a mammalian chromosome.
16. The genetic construct according to claim 15 wherein the eukaryotic chromosome is a human chromosome.
17. The genetic construct according to claim 16 wherein the nucleic acid molecule binds to CENP-A and -C or antibodies thereto.
18. The genetic construct according to claim 17 wherein the neocentromere is from human chromosome 10.
19. The genetic construct according to claim 18 wherein the neocentromere comprises a region between q24 and q26 on said human chromosome 10.
20. The genetic construct according to claim 18 wherein said chromosome is a human mardel (10) chromosome.

* * * * *